PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Shea N. Gardner et al	Examiner: Angela Bertagna
Serial No.:	10/727,779	Art Unit: 1637
Filed:	12/03/2003	Attorney Docket: IL-11191
TITLE:	SEQUENTIAL ADDITION OF SHORT DNA OLIGOS IN DNA-POLYMERASE-BASED SYNTHESIS REACTIONS	

Honorable Commissioner for Patents
Alexandria, VA 22313-1450

Attention: Board of Patent Appeals and Interferences

Dear Sir:

APPELLANT'S REPLY BRIEF (37 C.F.R. § 1.192)

This Reply Brief is submitted in response to the "Examiner's Answer" mailed April 1, 2009. One copy of the Reply Brief is being transmitted.

STATUS OF CLAIMS

The application as originally filed contained claims 1-17.

The claims on appeal are claims 11, 16, and 17.

The status of all the claims in the proceeding (*e.g.*, rejected, allowed or confirmed, withdrawn, objected to, canceled) is:

Claims 1-10 are withdrawn.

Claims 12-15 have been cancelled.

Claims 11, 16, and 17 are rejected.

Claims 11, 16, and 17 on appeal are reproduced in the Appendix of the Appeal Brief.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The Final Rejection mailed September 26, 2008 stated five (5) grounds of rejection. The five grounds of rejection are summarized as follows:

Grounds of Rejection #1 – Claim 16 was rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

Grounds of Rejection #2- Claim 11 was rejected under 35 U.S.C. § 102(e) as being anticipated by Evans.

Grounds of Rejection #3 - Claims 16 and 17 were rejected under 35 U.S.C. § 102(a) and 102(e) as being anticipated by Evans.

Grounds of Rejection #4 - Claims 11 and 17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Selifonov in view of Evans.

Grounds of Rejection #5 - Claim 16 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Selifonov in view of Evans and further in view of Murphy.

REPLY TO EXAMINER'S ANSWER REGARDING GROUNDS #1

(Claim 16 rejected under 35 U.S.C. § 112, first paragraph)

The Examiner's Answer contains the following statements in the second paragraph on page 13:

> "Applicant's arguments were not persuasive, because as discussed above, the original disclosure does not provide adequate support for claim 16 as amended. Prior to amendment, claim 16 required the use of starting oligonucleotides (oligos) of length n, wherein n is an odd number, having a length of n+l, *n+2, etc.* This claim language required the use of a mixture of starting oligos having lengths of n+l, *n+2, etc,* where n is an odd number. For example, this claim language encompassed an embodiment wherein a mixture of 5-mers, 6-mers, and so on (i.e. oligonucleotides having lengths of 5, 6, 7, *8, etc* nucleotides) are used as the starting oligos. The original disclosure provides support for the language "starting oligos of length n, wherein n is an odd number, of length n+l , *n+2, etc"* (see paragraphs 9, 63, and 64 of the specification, as noted by Applicant and in the previously made rejection reiterated above). However, amended claim 16 has a different scope compared to the previously presented version of the claim. Specifically, the recitation "starting oligos of length n+l or n+2" changes the scope

of the claim to require starting oligos of only one of the lengths (i.e. n+l or n+2), whereas the previous version of the claim required starting oligos having a plurality of different lengths (i.e. n+l and n+2, *etc).* "

The statements in the Examiner's Answer are respectfully traversed because claim 16 complies with the written description requirement of 35 U.S.C. § 112, first paragraph. Appellants' claim 16 states:

> "The method of producing a DNA molecule of user-defined sequence of claim 11 wherein said starting oligos of length n (n-mers) where n is an odd number are starting oligos of length n+1 or n+2."

There would be no question of support if claim 16 used the term "starting oligos of length n+1." Similarly, there would be no question of support if claim 16 used the term "starting oligos of length n+2." Therefore; there should be no question of support when claim 16 uses the term "starting oligos of length n+1 or n+2."

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116.

Appellants' original specification on page 6, lines 5-7 includes the following description of Appellants' starting oligos: "FIG. 7 illustrates another embodiment of a system of creating long DNA sequences, e.g., 1-10 kilobases, from short oligos of length n, n+1, n+2, etc. of the present invention." Appellants' original specification on page 11, lines 16-19 includes the following description of Appellants' assembly process: "The assembly process is substantially the same as the process called DNA shuffling. It is similar to PCR in that there is a template, a primer, a DNA polymerase, and the attendant nucleotides and buffers. It is

dissimilar to PCR in that the primer and template are the same entities – the 4-mers themselves."

One skilled in the art would reasonably conclude that the inventor had possession of the claimed invention because Appellants' original specification describes the assembly as "DNA shuffling" and the description of the Appellants' starting oligos as "short oligos of length n, n+1, n+2, etc." would be understood to include the claimed "starting oligos of length n+1 or n+2."

Appellants' claim 16 complies with the written description requirement of 35 U.S.C. § 112, first paragraph, because there is support in Appellants' original specification for the terms used in claim 16. The rejection of claim 16 in Grounds of Rejection #1 should be reversed.

REPLY TO EXAMINER'S ANSWER REGARDING GROUNDS #2
(Claim 11 rejected under 35 U.S.C. § 102(e) as being anticipated by Evans)

The Examiner's Answer contains the following statements in the second full paragraph on page 15:

> "The arguments presented at pages 17-19 are general in nature asserting that the Evans reference fails to teach the claimed method, but they offer no specific reasons as to why the reference is deficient. As discussed previously and reiterated above, Evans teaches all of the elements of the instant claim 11. Evans teaches *in vitro* assembly using a polymerase at paragraphs 58 & 68. Evans also teaches *in vitro* assembly by PCR, which inherently comprises parallel synthesis and shuffling using a DNA polymerase, at paragraphs 38, 93-98, and 195-199. Evans teaches that the *in vitro* assembly step is conducted by adding the sequence segments gradually in sequence order at paragraphs 58 and 62, for example. Evans further teaches temporal separation of the DNA sequence segments at paragraphs 58 and 62. Evans also teaches that the sequential addition minimizes errors (paragraph 66) and that computational techniques may be use to optimize (i.e. minimize errors) in the entire method (paragraph 178). Evans also teaches that the oligos used in the method have a length n, which is an odd number, and the use of oligos having a length of n+1 or n+2 (paragraphs 53, 58, & 82)."

The 35 U.S.C. § 102 rejection standard that "anticipation is established only when a single prior art reference discloses, either expressly or under principles of inherency, each and every element of a claimed invention" means that Appellants need only point out a single element of Appellant's claim 11 that is not found in the Evans reference. Appellants will point out several elements of Appellant's claim 11 not found in the Evans reference and the rejection should be reversed if even a single element of Appellant's claim 11 is not found in the Evans reference.

Appellants point out that the following claim element (step) of Appellant's claim 11 is not found in the Evans reference:

> **Assembling Said Groups Using DNA Shuffling**
> "assembling groups in vitro by assembling said groups into double-strand DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase."

The Evans reference does not show Appellants' claim 11 element/step Assembling Said Groups Using DNA Shuffling. The Examiner's Answer refers to paragraphs 38, 93-98, and 195-199 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 11.

Appellants point out that the following claim element (step) of Appellant's claim 11 is not found in the Evans reference:

> **Segments Added Gradually in Computationally Predicted Order**
> "said DNA sequence segments being added gradually, in an order that is predicted computationally to minimize errors to produce said DNA molecule of user-defined sequence."

The Evans reference does not show Appellants' claim 11 element/step Segments Added Gradually in Computationally Predicted Order. The Examiner's Answer refers to paragraphs 58 and 62 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 11.

Appellants point out that the following claim element (step) of Appellant's claim 11 is not found in the Evans reference:

> **Starting Oligos of Length n (n-mers) where n is an Odd Number**
> "wherein said step or assembling said groups into double-strand DNA molecules utilizes starting oligos of length n (n-mers) where n is an odd number."

The Evans reference does not show Appellants' claim 11 element/step Starting Oligos of Length n (n-mers) where n is an Odd Number. The Examiner's Answer refers to paragraphs 53, 58, & 82 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 11.

Since one or more of the above identified claim 11 elements described above are not found in the Evans reference, the Evans reference does not support a 35 U.S.C. § 102(e) rejection of Appellant's claim 11 and the rejection in Grounds of Rejection #2 should be reversed.

REPLY TO EXAMINER'S ANSWER REGARDING GROUNDS #3

(Claims 16 and 17 rejected under 35 U.S.C. § 102(a) and 102(e) as anticipated by Evans)

The Examiner's Answer contains the following statements in the third full paragraph on page 17:

> "Applicant's arguments regarding the teachings of Evans were not persuasive, because no specific evidence or arguments relating to the alleged deficiencies in the reference have been presented. The arguments presented at pages 19-22 are general in nature asserting that the Evans reference fails to teach the claimed methods, but they offer no specific reasons as to why the reference is deficient. As discussed previously and reiterated above, Evans teaches all of the elements of the instant claim 11., 16, and 17. The teachings of Evans with respect to claim 11 have been discussed above. Regarding claims 16 and 17, Evans teaches that the oligos used in the method have a length n, which is an odd number, and also the use of oligos having a length of n+l or n+2 (paragraphs 53, 58, & 82). Evans teaches variation of the oligo length and overlap between the fragments at paragraphs 53 and 54, which inherently results in the use of oligos that comprise multiple reading frames."

The 35 U.S.C. § 102 (a & e) rejection standard that "anticipation is established only when a single prior art reference discloses, either expressly or under principles of inherency, each and every element of a claimed invention" means that Appellants need only point out a single element of Appellant's parent claim 11 and dependent claims 16 and 17 that is not found in the Evans reference. Appellants will point out several elements of Appellant's parent claim 11 and dependent claims 16 and 17 not found in the Evans reference and the rejection should be reversed if even a single element of Appellant's parent claim 11 and dependent claims 16 and 17 is not found in the Evans reference.

Appellants point out that the following claim element (step) of Appellant's parent claim 11 is not found in the Evans reference:

> **Assembling Said Groups Using DNA Shuffling**
> "assembling groups in vitro by assembling said groups into double-strand DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase."

The Evans reference does not show Appellants' claim 11 element/step Assembling Said Groups Using DNA Shuffling. The Examiner's Answer refers to paragraphs 38, 93-98, and 195-199 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 11.

Appellants point out that the following claim element (step) of Appellant's parent claim 11 is not found in the Evans reference:

> **Segments Added Gradually in Computationally Predicted Order**
> "said DNA sequence segments being added gradually, in an order that is predicted computationally to minimize errors to produce said DNA molecule of user-defined sequence."

The Evans reference does not show Appellants' claim 11 element/step Segments Added Gradually in Computationally Predicted Order. The Examiner's Answer refers to paragraphs 58 and 62 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 11.

Appellants point out that the following claim element (step) of Appellant's parent claim 11 is not found in the Evans reference:

> **Starting Oligos of Length n (n-mers) where n is an Odd Number**
> "wherein said step or assembling said groups into double-strand DNA molecules utilizes starting oligos of length n (n-mers) where n is an odd number."

The Evans reference does not show Appellants' claim 11 element/step Starting Oligos of Length n (n-mers) where n is an Odd Number. The Examiner's Answer refers to paragraphs 53, 58, & 82 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 11.

Appellants point out that the following claim element (step) of Appellant's claim 16 is not found in the Evans reference:

> **Starting Oligos of Length n (n-mers) where n is an Odd Number**
> "wherein said starting oligos of length n (n-mers) where n is an odd number are starting oligos of length n+1 or n+2."

The Evans reference does not show Appellants' claim 16 element/step Starting Oligos of Length n (n-mers) where n is an Odd Number. The Examiner's Answer refers to paragraphs 53, 58, & 82 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 16.

Appellants point out that the following claim element (step) of Appellant's claim 17 is not found in the Evans reference:

Oligos in Multiple Reading Frames
"wherein said multiplicity of DNA sequence segments comprise oligos in multiple reading frames."

The Evans reference does not show Appellants' claim 17 element/step Oligos in Multiple Reading Frames where n is an Odd Number. The Examiner's Answer refers to paragraphs 53 & 54 of the Evans reference; however, these paragraphs do not disclose this claim element of Appellants' claim 17.

Since one or more of the above identified parent claim 11 and dependent claims 16 and 17 elements described above are not found in the Evans reference, the Evans reference does not support a 35 U.S.C. § 102(a & e) rejection of Appellant's claims 16 and 17 and the rejection in Grounds of Rejection #3 should be reversed.

REPLY TO EXAMINER'S ANSWER REGARDING GROUNDS #4
(Claims 11 and 17 rejected under 35 U.S.C. § 103(a) as unpatentable over Selifonov in view of Evans)

The Examiner's Answer on page 18 alleges that "Each of the limitations recited in the rejected claims is addressed by Selifonov and Evans."

Claim 11

The Examiner's Answer on page 19 alleges that Selifonov discloses:

> "(a) virtually preselecting a multiplicity of DNA segments that will comprise a user-defined DNA molecule by using computational techniques to virtually break the DNA molecule into virtual fragments of length n (n-mers), where n is an odd number (page 14, lines 20-29 and page 21, lines 12-22 teach using computational methods to virtually break the DNA molecule into virtual fragments; page 6, lines 8-10 teach using n-mers where n is an odd number)."

Appellants respectfully disagree. The cited portions of the Selifonov reference (Page 6, lines 8-10, Page 14, lines 20-29, and Page 21, lines 12-22) do not mention "n-mers where n is an odd number." The cited portions of the Selifonov

reference do not mention "using computational techniques to virtually break the DNA molecule into virtual fragments."

The cited portions of the Selifonov reference do not disclose Appellants' claim 11 limitations:

> "assembling groups in vitro by assembling said groups into double-strand DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase wherein said step of separating said DNA sequence segments temporally and said step of assembling said groups into double-strand DNA molecules of predetermined base-pairs is accomplished by said DNA sequence segments being added gradually, in an order that is predicted computationally to minimize errors to produce said DNA molecule of user-defined sequence."

> "wherein said step or assembling said groups into double-strand DNA molecules utilizes starting oligos of length n (n-mers) where n is an odd number."

Since these claim 11 limitations are missing from the Selifonov reference, the rejection in Grounds of Rejection #4 does not meet Criterion 1 of factually supporting a *prima facie* conclusion of obviousness and the rejection in the Grounds of Rejection #4 should be reversed.

The Examiner's Answer on page 19 alleges that Selifonov discloses:

> "(b) providing fragments of length n (n-mers) of defined size, where n is an odd number, that correspond to the virtual fragments (page 9, lines 23-31 and page 21, lines 12-30 teach providing fragments *in vitro* that correspond to the virtual fragments generated in step (a) above; page 6, lines 8-10 teaches using n-mess where n is an odd number in the synthesis method)."

Appellants respectfully disagree. The cited portions of the Selifonov reference (Page 6, lines 8-10, Page 9, lines 23-31 and Page 21, lines 12-30) do not mention "providing fragments of length n (n-mers) of defined size, where n is an odd number." The cited portions of the Selifonov reference do not mention "providing fragments *in vitro* that correspond to the virtual fragments generated in step (a) above."

The cited portions of the Selifonov reference do not disclose Appellants' claim 11 limitations:

> "assembling groups in vitro by assembling said groups into double-strand DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase wherein said step of separating said DNA sequence segments temporally and said step of assembling said groups into double-strand DNA molecules of predetermined base-pairs is accomplished by said DNA sequence segments being added gradually, in an order that is predicted computationally to minimize errors to produce said DNA molecule of user-defined sequence."

> "wherein said step or assembling said groups into double-strand DNA molecules utilizes starting oligos of length n (n-mers) where n is an odd number."

Since these claim 11 limitations are missing from the Selifonov reference, the rejection in Grounds of Rejection #4 does not meet Criterion 1 of factually supporting a *prima facie* conclusion of obviousness and the rejection in the Grounds of Rejection #4 should be reversed.

The Examiner's Answer on page 19 alleges that Evans discloses:

> "Evans teaches a method of synthesizing a user-defined nucleic acid sequence that anticipates the instant claims 11, 16, and 17, as discussed above."

> "Regarding claim 11, Evans teaches that addition of the oligonucleotides in a sequential order (optimized by computational modeling) minimizes reassembly errors (see paragraphs 58, 66, and 178). Specifically, Evans stated, "The sequential polynucleotide assembly methods of the invention further reduce the error rate observed with methods that require hybridization of pools of large numbers of oligonucleotides (paragraph 66)." Evans further stated, "The sequential polynucleotide assembly methods of the invention eliminate the need for purification. and allow for systematic assembly of identical sized double-stranded or single-stranded oligonucleotides (paragraph 66)."

Appellants respectfully disagree. The cited portions of the Evans reference (paragraphs 58, 66, and 178) do not disclose the following claim limitations of Appellants claims 11 and 16:

Assembling Said Groups Using DNA Shuffling

"assembling groups in vitro by assembling said groups into double-strand DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase."

Segments Added Gradually in Computationally Predicted Order
"said DNA sequence segments being added gradually, in an order that is predicted computationally to minimize errors to produce said DNA molecule of user-defined sequence."

Starting Oligos of Length n (n-mers) where n is an Odd Number
"wherein said step or assembling said groups into double-strand DNA molecules utilizes starting oligos of length n (n-mers) where n is an odd number."

Appellants have explained why the cited portions of the Evans reference do not disclose the claim limitations of Appellants claim 11 in the reply to Grounds of Rejection #2 above and those explanations are incorporated here rather than repeat the explanations.

Since these claim 11 limitations are missing from the Evans reference, the rejection in Grounds of Rejection #4 does not meet Criterion 1 of factually supporting a *prima facie* conclusion of obviousness and the rejection in the Grounds of Rejection #4 should be reversed.

Claim 17

The Examiner's Answer on page 19 alleges that Selifonov discloses:

"Regarding claim 17, Selifonov teaches that the multiplicity of DNA fragments comprises oligos in multiple reading frames. Specifically, Selifonov teaches variation of the oligo length and overlap between the fragments (page 33, lines 1-6). These DNA fragments inherently comprise multiple reading frames.

Appellants respectfully disagree. The cited portions of the Selifonov reference (Page 33, lines 1-6) do not mention "the multiplicity of DNA fragments comprises oligos in multiple reading frames."

The cited portions of the Selifonov reference do not disclose Appellants' claim 17 limitations:

> "wherein said multiplicity of DNA sequence segments comprise oligos in multiple reading frames."

Since these claim 17 limitations are missing from the references, the rejection in Grounds of Rejection #4 does not meet Criterion 1 of factually supporting a *prima facie* conclusion of obviousness and the rejection in the Grounds of Rejection #4 should be reversed.

No Reasons for Combining References

The Examiner's Answer on page 20 contains the following statements:

> "Applicant also argues that the rejection fails to provide a reason for combining the teachings of the cited references (page 28)."

> "This argument was not persuasive, because the rejection has provided a detailed discussion of the reasons an ordinary artisan would have been motivated to combine the teachings of the Selifonov and Evans references. Specifically, as discussed above, an ordinary artisan would have been motivated to utilize the *in* silica-optimized sequential addition of DNA fragments taught by Evans in the nucleic acid synthesis method of Selifonov, since Evans expressly taught that sequential addition of oligonucleotide segments in sequence order resulted in the following advantages: (1) a reduction in the assembly error rate, (2) elimination of the need for an extra purification step and (3) parallel synthesis of identical-sized nucleic acids (see paragraph 66). An ordinary practitioner of the nucleic acid synthesis method taught by Selifonov would have been motivated by the above teachings of Evans to sequentially add the fragments to the reassembly reaction in sequence order in order to improve the accuracy of the reassembly reaction, eliminate the need for *further* purification (thereby improving the speed and efficiency of the process), and obtain the ability to synthesize in parallel multiple, identically-sized nucleic acids."

The Examiner's Answer and the Final Rejection incorrectly attribute cited portions of the Evans reference and the Selifonov reference as disclosing Appellants claim limitations as discussed above. Appellants have explained that the cited portions of the Evans reference and the Selifonov reference do not

disclose multiple claim limitations of claims 11 and 17; therefore, the alleged "reasons for combining the references" in the Examiner's Answer and the Final Rejection are invalid.

The Examiner's Answer and the Final Rejection do not meet Criterion 3 of factually supporting a *prima facie* conclusion of obviousness and the rejection in the Grounds of Rejection #4 should be reversed.

REPLY TO EXAMINER'S ANSWER REGARDING GROUNDS #5

(Claim 16 rejected under 35 U.S.C. § 103(a) as unpatentable over Selifonov in view of Evans and further in view of Murphy)

The Examiner's Answer on page 22 alleges that the limitations of claim 16 are shown by the Selifonov and Murphy references with the following statements:

> "Selifonov teaches variation of DNA segment lengths and the use of a set of DNA segments comprising fragments of different lengths (see page 6, lines 8-10 and page 33, lines 1-6). However, Selifonov does not explicitly teach fragments of n+1 or n+2."
>
> "Murphy teaches a method of nucleic acid recombination. Briefly, the method of Murphy comprises primer extension and cleavage to create an "extension ladder" (column 4, lines 9-16) followed by recombinatorial synthesis to produce a mutagenized or chimeric nucleic acid (column 6, lines 34-40)."
>
> "Regarding claim 16, Murphy teaches that the "extension ladder" (a collection of DNA segments) may comprise sequences of different length, specifically, sequences different by one nucleotide increments (i.e. n, n+1 or n+2) (see column 6, lines 49-56). Regarding the differently sized sequences, Murphy stated, "Furthermore, the present invention may use a complete library of nucleic acid extension products that differ in length by a single base. As a result, recombinatorial mutagenesis results in recombined sequences with potential crossover points at every single nucleotide in a nucleic acid sequence (column 3, line 66 - column 4, line 4)."

Appellants respectfully disagree. The cited portions of the Selifonov and Murphy references do not disclose Appellants' claim 16 limitations:

> "wherein said starting oligos of length n (n-mers) where n is an odd number are starting oligos of length n+1 or n+2."

Since these claim 16 limitations are missing from the Selifonov reference and Murphy reference, the rejection in Grounds of Rejection #5 does not meet Criterion 1 of factually supporting a *prima facie* conclusion of obviousness and the rejection in the Grounds of Rejection #5 should be reversed.

No Reasons for Combining References

The Examiner's Answer on pages 22-23 contains the following statements:

> "Applicant also argues that the rejection fails to provide a reason for combining the teachings of the cited references (page 33)."

> "This argument was not persuasive, because the rejection has provided a detailed discussion of the reasons an ordinary artisan would have been motivated to combine the teachings of the Selifonov, Evans, and Murphy references. Specifically, as discussed previously and above, an ordinary artisan would have been motivated to utilize DNA fragments differing by one nucleotide in length (i.e. oligonucleotides of length n+1 or n+2, *etc)* in the recombination method resulting from the combined teachings of Selifonov and Evans, since Murphy expressly taught that such a fragment pool resulted in "recombined sequences with potential crossover points at every single nucleotide in a nucleic acid sequence (column 3, line 66 - column 4, line 4)." An ordinary practitioner of the method resulting from the combined teachings of Selifonov and Evans would have been motivated by these teachings of Murphy to utilize the above length-diverse fragment pool in order to maximize the diversity of the resulting recombined/reassembled sequences, thereby improving the method's ability to generate nucleic acids encoding proteins with improved functional properties."

The Examiner's Answer and the Final Rejection incorrectly attribute cited portions of the Selifonov reference, the Evans reference, and the Murphy reference as disclosing Appellants claim limitations as discussed above. Appellants have explained that the cited portions of the three references do not disclose multiple claim limitations of claim 16; therefore, the alleged "reasons for combining the references" in the Examiner's Answer and the Final Rejection are invalid.

The Examiner's Answer and the Final Rejection do not meet Criterion 3 of factually supporting a *prima facie* conclusion of obviousness and the rejection of claim 16 in the Grounds of Rejection #5 should be reversed.

Summary

Appellants' specification contains an adequate written description of the terms used in the claims and Appellants' specification complies with the requirements of 35 U.S.C 112, first paragraph.

Appellants' invention is not anticipated by the references and Appellants' claims are unobvious over the references cited in the Final Rejection and the Examiner's Answer. The Examiner's Answer incorrectly attributes cited portions of the references as disclosing Appellants claim limitations; however, a detailed reading of the cited portions of the references demonstrates that the Appellants' claim limitations are missing from the references.

The rejection of Appellants' claims on appeal should be reversed.

It is respectfully requested that Appellants' claims 11, 16, and 17 on appeal be allowed.

Respectfully submitted,

By: _____

Eddie E. Scott
Lawrence Livermore National Laboratory (LLNL)
7000 East Avenue, Mail Code L-703
Livermore, CA 94550
Attorney for Appellants
Registration No. 25,220
Telephone No. (925) 424-6897

Date: 5/1/2009